51

WE CLAIM:

1.   A method for identifying a marker of an abnormal physiological condition in an individual, which method comprises:

(i)   providing a biological sample from the individual;

5   (ii)   subjecting the sample to one or more separation steps to resolve one or more glycoconjugates from other components in the sample;

(iii)   treating the one or more glycoconjugates to release glycans;

(iv)   analysing the released glycans by mass spectrometry to produce a glycosylation profile; and

10 (v)   analysing the glycosylation profile for changes in a glycan marker which is indicative of the abnormal physiological condition.

2.   The method of claim 1, wherein the glycoconjugate is a high molecular weight glycoprotein, a proteoglycan or a glycolipid.

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3.   The method of claim 1 wherein step (v) comprises comparing the glycosylation profile produced in step (iv) with a control glycosylation profile.

4.   A method for identifying a glycoconjugate whose levels are altered in an
20 individual suffering from an abnormal physiological condition, which method comprises:

(i)   providing a biological sample from the individual;

(ii)   subjecting the sample to one or more separation steps to resolve one or more glycoconjugates from other components in the sample;

25 (iii) treating the one or more glycoconjugates to release glycans;

(iv)   analysing the released glycans by mass spectrometry to produce a glycosylation profile;

(v)   comparing the profile with a control profile.

(vi)   identifying a glycan whose levels are altered in the profile obtained in step (iv)
30 as compared with the control profile; and

(vii)   identifying a glycoconjugate present in the biological sample from which the glycan is derived.

5.   A method for identifying a glycan which is a diagnostic marker for an abnormal
35 physiological condition, which method comprises:

(i)   providing a biological sample from an individual suffering from an abnormal physiological condition;

(ii)   subjecting the sample to one or more separation steps to resolve one or more glycoconjugates from other components in the sample;

5   (iii)   treating the one or more glycoconjugates to release glycans;

(iv)   analysing the released glycans by mass spectrometry to produce a glycosylation profile; and

(v)   identifying a glycan whose levels are altered in the profile obtained step (iv) as compared with a control profile, the identified glycan being the diagnostic marker.

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6.   A method for identifying a glycoconjugate which is a diagnostic marker for an abnormal physiological condition, which method comprises:

(i)   providing a biological sample from an individual suffering from an abnormal physiological condition;

15 (ii)   subjecting the sample to one or more separation steps to resolve one or more of glycoconjugates from other components in the sample;

(iii)   treating the one or more of glycoconjugates to release glycans;

(iv)   analysing the released glycans by mass spectrometry to produce a glycosylation profile;

20 (v)   identifying a glycan whose levels are altered in the profile obtained step (iv) as compared with a control profile; and

(vi)   identifying a glycoconjugate present in the biological sample from which the glycan is derived, the identified glycoconjugate being the diagnostic marker.

25 7.   The method according to any one of claims 1 to 6 wherein the abnormal physiological condition is a pathogenic infection, a malignancy or a respiratory disorder.

8.   The method of claim 7 wherein the malignancy is ovarian cancer.

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9.   The method of claim 7 wherein the abnormal physiological condition is an acute pulmonary exacerbation in a subject suffering from cystic fibrosis.

10.   The method of claim 7 wherein the respiratory disorder is cystic fibrosis.

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11.   A method of identifying a cancer marker comprising:

(i)   obtaining a blood fraction from a human or animal subject having a cancer and from a healthy human or animal;

(ii)   subjecting the blood fractions to one or more separation steps to resolve one or more glycoconjugates from other components in the sample;

5   (iii)   treating the one or more glycoconjugates from each blood fraction to release glycans;

(iv)   comparing the profile of molecular species obtained from the fractions; and

(v) identifying those molecular species having a modified level, wherein a modified level of said molecular species indicates that the molecular species is a cancer marker.

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12.   A method of identifying a cystic fibrosis (CF) marker comprising:

(i)   obtaining sputum or saliva from a CF patient having an acute pulmonary exacerbation and from a non-CF subject or a CF patient that does not have an acute pulmonary exacerbation;

15   (ii)   subjecting the sputum or saliva to one or more separation steps to resolve one or more high molecular weight glycoproteins from other components in the sample;

(iii)   treating the one or more high molecular weight glycoproteins from each subject to release glycans;

(iv)·   comparing the profile of molecular species obtained from the subjects; and

20   (v)   identifying those molecular species having a modified level between a CF patient having an acute pulmonary exacerbation and either a non-CF subject or a CF patient that does not have an acute pulmonary exacerbation, wherein a modified level of said molecular species indicates that the molecular species is a CF marker.

25   13.   The method according to any one of claims 1 to 12 wherein a separation step comprises performing a process selected from the group consisting of electrophoresis and chromatography.

14.   The method of claim 13 wherein wherein a separation step comprises
30   performing electrophoresis.

15.   The method of claim 14 wherein the electrophoresis is one-dimensional SDS-agarose/polyacrylamide gel electrophoresis (1D SDS-AgPAGE).

35   16.   The method of claim 14 wherein the electrophoresis is two-dimensional gel electrophoresis.

17.   The method according to any one of claims 1 to 16 wherein the glycoconjugates are subjected to digestion with PNGase F.

18.   The method according to any one of claims 1 to 16 wherein the glycoconjugates
5   are subjected to reductive β-elimination to release the glycans.

19.   A cancer marker comprising an oligosaccharide comprising a structure selected from the group consisting of:
(i)NeuAc-(Hex-)HexNAc;
10 (ii)NeuAc-Hex-HexNAc;
(iii) Hex-(Hex-HexNAc-)HexNAc;
(iv) NeuAc-Hex-(NeuAc-)HexNAc;
(v) Hex-(Hex-HexNAc-)HexNAc + NeuAc;
(vi)Hex-HexNAc +NeuAc$_3$;
15 (vii) Hex-(Hex-HexNAc-)HexNAc + NeuAc$_2$;
(viii)Hex$_2$HexNAc$_2$(SO$_3$H)$_1$;
(ix) Hex$_2$HexNAc$_2$NeuAc;
(x) Hex$_2$HexNAc$_2$NeuAc(SO$_3$H);
(xi) DeoxyHex$_1$Hex$_2$HexNAc$_2$NeuAc(SO$_3$H);
20 (xii) Hex$_2$HexNAc$_2$NeuAc$_2$;
(xiii) DeoxyHex$_1$Hex$_2$HexNAc$_2$NeuAc;
(xiv) Hex$_2$HexNAc$_2$NeuAc$_2$(SO$_3$H)
or a part thereof.

25 20.   A cancer marker comprising an oligosaccharide that comprises two or more linked sialic acid residues.

21.   The cancer marker of claim 20 comprising an O-linked oligosaccharide.

30 22.   The cancer marker of claim 20 or 21 wherein said marker is a disialylated oligosaccharide or trisialylated oligosaccharide.

23.   The cancer marker according to any one of claims 20 to 22 comprising the structure Hex-HexNeuAc-NeuAc$_3$.
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24.   The cancer marker according to any one of claims 19 to 23 wherein said marker is an ovarian cancer marker.

25.   A method for diagnosing cancer comprising detecting the presence of a cancer marker in a biological sample from a human or animal subject, wherein the cancer marker comprises an oligosaccharide comprising a structure selected from the group consisting of: (i)NeuAc-(Hex-)HexNAc;
(ii)NeuAc-Hex-HexNAc;
(iii) Hex-(Hex-HexNAc-)HexNAc;
(iv) NeuAc-Hex-(NeuAc-)HexNAc;
(v) Hex-(Hex-HexNAc-)HexNAc + NeuAc;
(vi)Hex-HexNAc +NeuAc$_3$;
(vii) Hex-(Hex-HexNAc-)HexNAc + NeuAc$_2$;
(viii)Hex$_2$HexNAc$_2$(SO$_3$H)$_1$;
(ix) Hex$_2$HexNAc$_2$NeuAc;
(x) Hex$_2$HexNAc$_2$NeuAc(SO$_3$H);
(xi) DeoxyHex$_1$Hex$_2$HexNAc$_2$NeuAc(SO$_3$H);
(xii) Hex$_2$HexNAc$_2$NeuAc$_2$;
(xiii) DeoxyHex$_1$Hex$_2$HexNAc$_2$NeuAc;
(xiv) Hex$_2$HexNAc$_2$NeuAc$_2$(SO$_3$H)
or a part thereof.

26.   A method for diagnosing cancer comprising detecting the presence of a cancer marker in a biological sample from a human or animal subject, wherein the cancer marker comprises an oligosaccharide that comprises two or more linked sialic acid residues.

27.   The method of claim 26 wherein the cancer marker that is detected is a disialylated oligosaccharide or trisialylated oligosaccharide.

28.   The method of claim 26 or 27 wherein the cancer marker that is detected has the structure Hex-HexNeuAc-NeuAc$_3$.

29.   The method according to any one of claims 25 to 28 wherein the cancer is ovarian cancer.

56

30.   The method according to any one of claims 25 to 29 wherein the biological sample comprises blood or serum.

31.   The method according to any one of claims 25 to 30 wherein the cancer marker
5   is detected by mass spectrometry.

31.   The method according to any one of claims 25 to 30 wherein the cancer marker is detected by a process comprising contacting an affinity ligand that binds to the cancer marker with the sample for a time and under conditions sufficient for binding to
10   occur and then detecting the binding.

32.   The method of claim 31 wherein the affinity ligand is an antibody.

33.   The method of claim 31 wherein affinity ligand is a lectin or selectin.
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34.   The method according to any one of claims 25 to 30 wherein the cancer marker is detected by a process comprising staining the cancer marker with a dye that binds to the cancer marker.

20   35.   A method for identifying a candidate therapeutic target, which method comprises:
        (i)   providing a biological sample from an individual suffering from an abnormal physiological condition;
        (ii)   subjecting the sample to one or more separation steps to resolve one or more of
25   glycoconjugates from other components in the sample;
        (iii)   treating the one or more of glycoconjugates to release glycans;
        (iv)   analysing the released glycans by mass spectrometry to produce a glycosylation profile; and
        (v)   identifying a glycan whose levels are altered in the profile obtained in step (iv)
30   as compared with a control profile, the identified glycan being the identified candidate therapeutic target.

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36.   A method for identifying a candidate therapeutic target, which method comprises:

(i)   providing a biological sample from an individual suffering from an abnormal physiological condition;

5   (ii)   subjecting the sample to one or more separation steps to resolve one or more glycoconjugates from other components in the sample;

(iii)   treating the one or more of glycoconjugates to release glycans;

(iv)   analysing the released glycans by mass spectrometry to produce a glycosylation profile; and

10   (v)   identifying a glycan whose levels are altered in the profile obtained in step (iv) as compared with a control profile; and

(vi)   identifying a glycoconjugate present in the biological sample from which the glycan is derived, the identified glycoconjugate being the identified candidate therapeutic target.